

**REMARKS**

The Office Action and the cited and applied references have been carefully reviewed. Claims 2-7, 13-15, and 17-27 presently appear in this application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

For the record, claims 26 and 27 which were newly added by the amendment filed June 17, 2004 (resent by fax on October 15, 2004), presently appear in this application even though they do not appear to be indicated as pending on the Summary page of the Office Action dated January 7, 2005.

The face-to-face interview among Dr. Fredriksson, one of the present inventors, and the undersigned, representing applicants, and Examiners Chunduru and Fredman, on March 10, 2005, is hereby gratefully acknowledged. The undersigned wishes to thank the examiners for the courtesies extended during this interview.

At the interview, the amendment to claim 14 to overcome the indefiniteness issue and the proposed recitation in claim 25 that each proximity probe comprises nucleic acids acting as a reactive functionality coupled to the binding

moiety, as now amended in the instant amendment, were discussed. Also discussed was the filing of a declaration under 37 CFR 1.132 with a showing of unexpected results to overcome the §103(a) obviousness rejection. The arguments presented at the interview are incorporated herein.

Claims 14-15 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The examiner indicates that amendment of claim 14 to read "which interacts/which binds" would obviate this rejection. The examiner's suggestion is adopted, thereby obviating this rejection.

Claims 2-7, 13-15, and 17-27 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Landegren (WO 97/00446) in view of Ebersole et al. (WO 97/32044). The examiner indicates that Landegren teaches the detection of analyte on a solid support but does not teach the detection of analyte in solution or not immobilized on a solid support. However, the examiner cites and applies Ebersole et al. as a secondary reference for its teaching (i.e., page 17, lines 19-31 and page 19, lines 1-7) of a homogeneous detection probe system (HDPS) which requires detection without immobilization of the analyte/probe. This rejection is respectfully traversed.

As can be seen from Figure 13 of Ebersole, which schematically illustrates the homogeneous detection probe system, it is clear there is no signal when the probes F1 and F2 (a fluorophore and quencher) are in close proximity to each other but that there is signaling and detection of analyte (target) when the probes are no longer in close proximity. This is completely opposite to the presently claimed invention, where the presence of analyte is only detected when the proximity probes are in close proximity and allows for interaction between the nucleic acids on the probes. Accordingly, Ebersole actually teaches away from the present invention and therefore simply cannot be combined with the disclosures and teachings of the applied Landegren reference to lead one of ordinary skill in the art to the present invention. This is especially true because claim 25 is amended to recite that each (or in otherwords, all) proximity probe comprises nucleic acids acting as a reactive functionality coupled to the binding moiety.

In addition, attached hereto is an executed declaration under 37 CFR 1.132, which compares results obtained with the solid phase anchored proximity ligation assay of the applied Landegren reference (WO 97/00446) and with the presently claimed homogeneous liquid phase proximity ligation assay. As demonstrated by the experimental results

presented in the attached declaration, the present inventors have discovered unexpectedly superior results which are clearly unobvious over the cited and applied Landegren and Ebersole references. The presently claimed method provides a significantly lower limit of detection for the analyte while requiring much less amounts (by many orders of magnitude) of proximity probes than the solid phase assay of the cited and applied Landegren reference. Furthermore, the presently claimed method eliminates/omits more than one step of the solid phase assay method of Landegren, i.e., the immobilizing antibodies/analyte to a solid support step(s) and the washing step(s) to remove unbound proximity probes. Thus, pursuant to MPEP 2144.04 II(B), the omission of an element (step) and retention of its function is an indicia of unobviousness. Accordingly, the presently claimed invention cannot be made obvious by the cited and applied Landegren reference alone or in combination with the Ebersole et al., reference.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Applicants are attaching SB08 form (substitute for form 1449) listing U.S. Patent No. 6,511,809 (Baez et al.) and request that this be made of record in the present application even though this U.S. patent is not available as prior art.

Appln. No. 09/785,657  
Amd. dated March 28, 2005  
Reply to Office Action of January 7, 2005

It is further requested that the examiner initial the SB08 form and return an initialed copy with the next Office Action. ✓

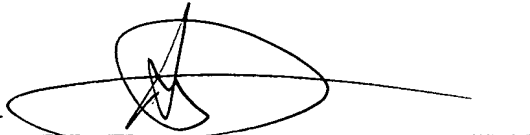
In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

In the event that any issue still needs to be resolved for the claims or the application to be placed in condition for allowance, it is hereby requested that the examiner contact the undersigned by telephone in order to expedite prosecution.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.  
Attorneys for Applicants

By

A handwritten signature in black ink, appearing to be 'Allen C. Yun', is written over a horizontal line. The signature is stylized with a large loop and a cross-like shape in the center.

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**Complete if Known**

Application Number	09/785,657
Filing Date	February 20, 2001
First Named Inventor	Ulf LANDEGREN et al.
Group Art Unit	1637
Examiner Name	S. Chunduru
Attorney Docket Number	LANDEGREN=1A

U.S. PATENT DOCUMENTS

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## FOREIGN PATENT DOCUMENTS

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Examiner  
Signature

Date  
Considered

\* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kind Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.